PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification [4] : A61M 5/14	A1	(11) International Publication Number: WO 88/ 05314
		(43) International Publication Date: 28 July 1988 (28.07.88)

(21) International Application Number: PCT/EP88/00062

(22) International Filing Date: 27 January 1988 (27.01.88)

(31) Priority Application Number: 8701731

(32) Priority Date: 27 January 1987 (27.01.87)

(33) Priority Country: GB

(71) Applicant *(for all designated States except US)*: KABIVITRUM AB [SE/SE]; Lindhagensgatan 133, S-112 87 Stockholm (SE).

(72) Inventors; and

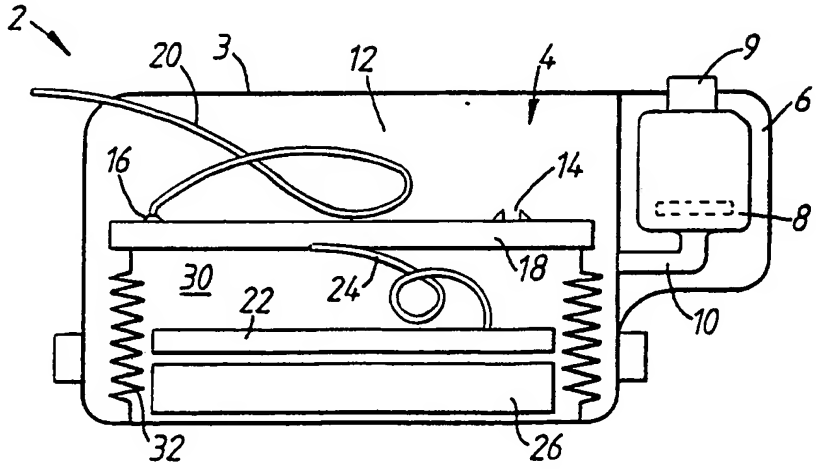
(75) Inventors/Applicants *(for US only)* : LABBE, Jean-Marie [BE/BE]; Avenue des combattants 99, B-1488 Bousval (BE). DAMHUIS, Edward, Hendrikus, Johannes [NL/BE]; Rue Bruyere Del Vigue 19, B-1488 Bousval (BE). COX, Robert, Edward, Latimer [GB/FR]; 3, allée Traversière, Domaine de Grandchamp, F-78230 Le Pecq (FR).

(74) Agent: A.A. THORNTON & CO.; Northumberland House, 303-306 High Holborn, London WC1V 7LE (GB).

(81) Designated States: AT (European patent), AU, BE (European patent), CH (European patent), DE (European patent), DK, FI, FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), NL (European patent), NO, SE (European patent), US.

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: A PUMP AND A FLUID DISPENSING DEVICE INCORPORATING A PUMP



(57) Abstract

A pump (2) for use in an implantable drug delivery system for ambulatory patients meets the requirement for small size by comprising a piezoelectric disc element bonded to a diaphragm member forming one wall of a pump chamber (18), and a battery (26) and electrical circuits (22) for cyclically applying electrical voltage to the piezoelectric member whereby to induce pumping movement in the diaphragm member to pump drugs from a reservoir (12) via a valve (14) to a delivery catheter (20) via a valve (16). A gas spring (30) is provided to move the pump (18) to maintain adequate pressure in the drug reservoir.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	**FR**	France	**ML**	Mali
AU	Australia	**GA**	Gabon	**MR**	Mauritania
BB	Barbados	**GB**	United Kingdom	**MW**	Malawi
BE	Belgium	**HU**	Hungary	**NL**	Netherlands
BG	Bulgaria	**IT**	Italy	**NO**	Norway
BJ	Benin	**JP**	Japan	**RO**	Romania
BR	Brazil	**KP**	Democratic People's Republic of Korea	**SD**	Sudan
CF	Central African Republic			**SE**	Sweden
CG	Congo	**KR**	Republic of Korea	**SN**	Senegal
CH	Switzerland	**LI**	Liechtenstein	**SU**	Soviet Union
CM	Cameroon	**LK**	Sri Lanka	**TD**	Chad
DE	Germany, Federal Republic of	**LU**	Luxembourg	**TG**	Togo
DK	Denmark	**MC**	Monaco	**US**	United States of America
FI	Finland	**MG**	Madagascar		

A PUMP AND A FLUID DISPENSING DEVICE INCORPORATING A PUMP

This invention relates to pumps of a small size particularly though not exclusively implantable pumps which are sufficiently small for use within the human body.

Pumps of small dimensions are used in implantable drug dispensing devices where a medicament is to be dispensed to an ambulatory patent on a regular or intermittent basis over an extended period of time, as where insulin is dispensed in the treatment of diabetes, or where chemotherapeutic drugs are dispensed in the treatment of cancer. In these circumstances it is advantageous in the treatment with the drug to perform an automatic dispensation o the drug without having to rely upon pills or injections. Thus a unit is implanted within the patient comprising a reservoir of the drug and a pump, the pump being under control of a control circuit which may be coupled by an electromagnetic transmitter and receiver to an external control source.

Such a device for delivering the drug must be reliable in operation, sealed against body fluids and must hold a sufficient quantity of medication so as to avoid the need for frequent refills and must be refillable when empty. Furthermore, such dispensing systems must be physically small so as to be readily implantable without unnecessary disturbance of the baby.

It is known to employ in such dispensing devices pumps such as the peristaltic type or solenoid type. Peri-

staltic pumps operate by responding to blood pressure within the body and solenoid pumps operate under control of an internal battery connected to a solenoid for operating a suitable pump mechanism. However such pumps are relatively large and considering their size, are inefficient within the context of implantable units.

The present invention is based on the concept of a pump which incorporates a mechanism which is actuated by means of a piezo electric element. Such a pump can be made of a very small size and is therefore suitable for use in an implantable drug delivery system. However such a pump may be of use in whatever application where the requirement is for a pump of very small size.

The present invention therefore provides in general terms a pump comprising a source of electric power connected to means for cyclically applying electrical voltage to a piezo electric element whereby to induce periodic changes in dimension in the piezo electric element, the piezo electric element being physically contiguous with and directly coupled to a movable pump element whereby changes in dimension of the piezo electric element induces pumping movement into the movable pump member.

Thus since all that is required to provide the pump motive power is a piezo electric element and a source of electrical power such as for example a battery, and that furthermore since the piezo electric element is contiguous with and directly coupled with the movable pump element, with no intervening shaft or push rod, the piezo electric pump may be made very small in dimensions.

The electrical power supplied to the piezo electric element from the battery may be in pulsed d.c. form or alternatively and as preferred for efficiency it may be AC, with a suitable inverter circuit being provided.

The movable pump member may be of any suitable type, rotatable or displaceable, and the piezo electric element

may be coupled to the pump member in such a way as to induce the required type of movement. In a preferred embodiment, the movable pump member comprises a flexible membrane movement of which increases or decreases the size of a pump chamber which is coupled to a drug reservoir and an outlet port by suitable one way valves. Thus a decrease in volume of the pump chamber causes a drug within the pump chamber to be expelled through the valve of the outlet port, the valve at the inlet port remaining closed, whereas when the volume of the pump chamber is increased by movement of the membrane. the one way valve at the outlet port is closed whereas the one way valve at the inlet port is opened to permit further drug to be introduced into the pump chamber. As preferred the piezo electric element comprises a planar element extending over a substantial or major part of the surface area of the membrane and being firmly affixed to the surface thereof. Thus when dimensional changes are induced in a suitable direction in the piezo electrical element, this causes the piezo electric element to curve in one or two opposite directions from the plane in which it is disposed and the consequent bowing effect of the element causes a corresponding deformation of the membrane resulting in similar type of movement of the membrane. Thus the pump may be configured as essentially a flat disc-like element, with the piezo electric element, the membrane forming the movable pump member and the pump chamber all being of essentially planar form.

A preferred embodiment of the invention will now be described with reference to the accompanying drawings wherein:

Figure 1 is a view in elevation of the exterior of an implantable dispenser incorporating a pump according to the invention;

Figure 2 is a schematic cross-sectional view of the dispenser of Figure 1;

Figure 3 is a view in cross-section of the pump of

the implantable dispenser; and

Figure 4 is a block diagram of the electrical control circuit of the implantable dispenser.

Referring now to the drawings there is shown an implantable dispenser 2 for use in a drug delivery system where the dispenser is implanted into the body of a human being and is operative to dispense into the body suitable quantities of a drug at intervals under control of a circuit within the dispenser and as required under external control by means of a receiver/transmitter arrangement. The dispenser 2 as shown in Figure 1 comprises an outer casing 3 of bio-compatible material, for example titanium alloy or stainless steel or biologically compatible silicone rubber. The dispenser body comprises a main portion 4 which is circular in elevation with a diameter of 3.5 cm (this dimension and the dimensions quoted below are approximate). The depth of the main portion 4 is 2.5 cm. A lobe portion 6 is provided having a width as measured from the circumference of the circular portion 4 of 1.5 cm and having a depth of 1.5 cm.

The overall configuration of the implantable dispenser is shown in Figures 2 and 3 as comprising a septum 8 mounted in lobe portion 6 and containing a radially compressed block of silicone rubber, an inlet 9 being provided for external access and a passageway 10 to a main drug reservoir region 12. In use, the reservoir 12 is filled by insertion of the hypodermic needle of a syringe into the silicone rubber insert via a passageway 9, so that the drug flows into the main reservoir region 12 via a passageway 10. Extraction of the needle when the reservoir is filled automatically closes the silicone block. Valves 14. 16 are provided, inlet valve 14 permitting entry of the drug into a pump 18 and outlet valve 16 permitting exit of the drug from the pump body to a delivery catheter 20 which extends from the dispenser body to a suitable location within the

human body. The pump is connected to an electronic control circuit by means of electrical leads 24, the electronic circuit being powered by a battery 26. A gas spring is provided in the area 30 between the pump and the electronic circuit 22 within the volume enclosed by a bellows 32. The function of the gas spring is to maintain an essentially constant pressure in reservoir 12 as the quantity of drug decreases during infusion. By selecting a suitable mixture of "Freon"-type hydrocarbons which liquify at about one bar pressure, the pressure in the gas spring can be made to remain effectively constant (apart from the spring characteristics of the bellows) as the drug is used up and the bellows 32 opens.

The pump is shown in more detail in Figure 3 as being of generally flat and planar shape being 3.0 cm in diameter and 2 mm thick. Thepump comprises two plate members 30, 32 of pressure moulded titanium alloy and an intermediate plate 34 is also formed of titanium alloy. These plates define a port 36 for inlet valve 14 housing a freely movable valve member 38 and communicating with a passageway 40. Passageway 40 formed in intermediate plate 34 communicates with a pump chamber 42 and a further channel 44 formed in plate member 34 communicates with an outlet valve having a freely movable valve member 46 which is mounted in a recess 48 which communicates with outlet 50.

Titanium plate 32 defines a movable member to which is bonded a circular plane piezo electric sheet 52. Suitable seals are provided (not shown) surrounding the valve members, the seals and valve members being made of biologically compatible materials, for example silicone rubber. The three plates 30, 32, 34 are sealed together by a technique such as electron beam welding or diffusion bonding. The piezo electric element 52 is mounted on plate 32 using a conductive epoxy filled with silver.

In operation, when an electric voltage is applied across the thickness of the piezo electric element 52. this

creates a bowing, resulting in the central part of the piezo electric element moving out of the plane of the element a certain amount whereby to cause a corresponding deformation in plate 32 and thus causing an expansion or contraction of volume of the pump chamber. Where expansion is caused, this creates a suction effect causing valve member 38 to be moved downwardly allowing drug from reservoir 12 to flow into the valve chamber. Outlet valve member 46 is maintained against passage 44 during this movement. Upon contraction of the space of the pump chamber caused by inward movement of plate 32, valve member 46 is pushed upward by permitting a drug to flow through the outlet valve 16.

Referring now to Figure 4 there is shown the electronic circuitry for controlling the pump comprising an inductive loop antenna 60 which receives electrical signals from external control apparatus. This is connected to a receiver and transmitter 62, 64 which in turn provide and receives signals from a central control logic 66. A lithium battery 26 is coupled via a battery checking circuit 68 to control logic 66. Electronics circuits 70 are provided coupled to sensors which are situated within the pump to monitor conditions such as battery charge, critical operating voltages, internal humidity, pump/valve monitoring, quantity of drug in reservoir and rate of dispensation, clock settings and stored operating system. In addition sensors may be situated at parts of the human body to determine from biological conditions whether a drug should be administered. The control logic is also coupled to an oscillatory driver 72 which includes an inverter circuit and which provides alternating current to the pump for causing a pumping action of the pump. It may thus be seen that the pump can be controlled in any suitable manner to provide a regular or intermittent flow or drug to a person having this dispenser device implant-therewithin, the pump being controlled either internally by sensor devices mounted

within the patient or externally by means of signals transmitted electromagnetically from an external control device.

The pump as described delivers very small quantities of fluid, as shown about 0.1 micro litres per pump sample. The advantages of the pump as described are its very small size and its cheapness as compared with peristaltic pumps or solenoid pumps and the pump is therefore very suitable for applications where accurate quantities of liquid must be pumped in small amounts and where a pump of small size is required.

CLAIMS:

1. A pump comprising a piezoelectric element (52) physically contiguous with and directly coupled to a movable pump element (32) whereby changes in dimension of the piezoelectric element induces pumping movement in the movable pump element, and a source of electrical power (26) connected to control means (22) for cyclically applying electrical voltage to the piezoelectric element (52) whereby to induce periodic changes in dimension in a piezoelectric element.

2. A pump as claimed in claim 1, wherein the movable pump element (32) comprises a flexible diaphragm forming part of the wall of a pump chamber (42).

3. A pump as claimed in claim 2, and comprising a one way valve member (38) being connected between a fluid reservoir (12) and the pump chamber (42) to permit flow of a fluid from the reservoir into the pump chamber upon movement of the flexible diaphragm (32).

4. A pump as claimed in claim 3, including a further one way valve member (46) connected between the pump chamber (42) and an outlet (50).

5. A pump as claimed in any one of claims 2, 3 or 4, wherein the source of electric power is a battery in the shape of a disc and the control means (22) in the shape of a planar member, wherein the battery, control circuit and pump chamber are stacked one upon another to permit the pump to be formed as a disc-like device.

6. A pump as claimed in any preceding claim, wherein the control means (22) includes receiver means arranged to respond to remotely transmitted electromagnetic waves to actuate the pump.

7. A pump as claimed in claim 6, and including means for checking the condition of the source of electric power.

8. A dispensing device comprising a housing (3) forming a reservoir (12) for fluid to be dispensed and a pump (18) located within the reservoir (12) for dispensing the fluid, the pump being constructed in accordance with any one of the preceding claims.

9. A dispensing device according to claim 8 and comprising means (32) for maintaining constant the pressure of fluid in the reservoir as the fluid is being dispensed.

10. A dispensing device according to claim 9, wherein the pressure maintaining means comprises an expandable member (32) within the reservoir.

11. A dispensing device according to claim 10, wherein the pump (18) is disposed within the expandable member (32).

12. A dispensing device according to any one of claims 8 to 11, and comprising an inlet chamber (8) connected to the reservoir (12) and sealed by an elastomeric member (9) whereby to permit injection of fluid into the reservoir by means of an hypodermic syringe.

1/2

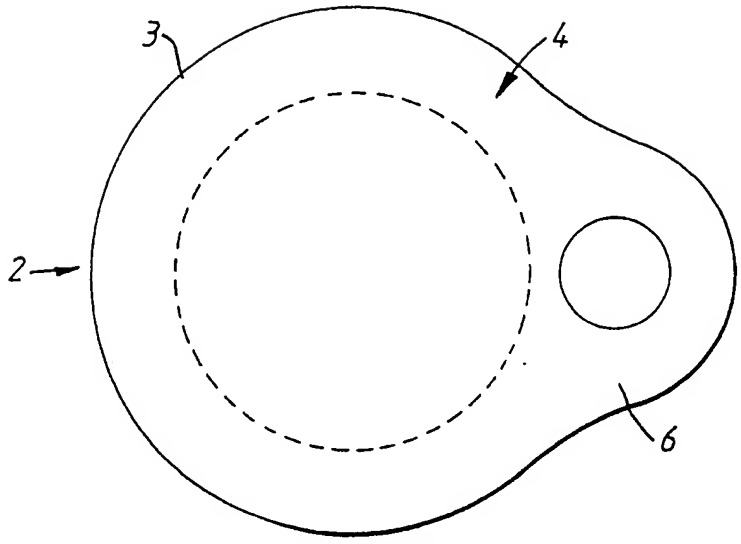


FIG. 1.

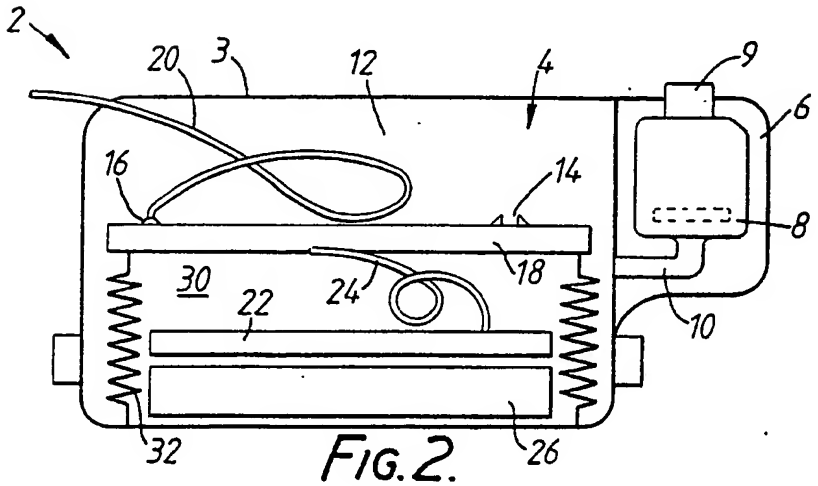


FIG. 2.

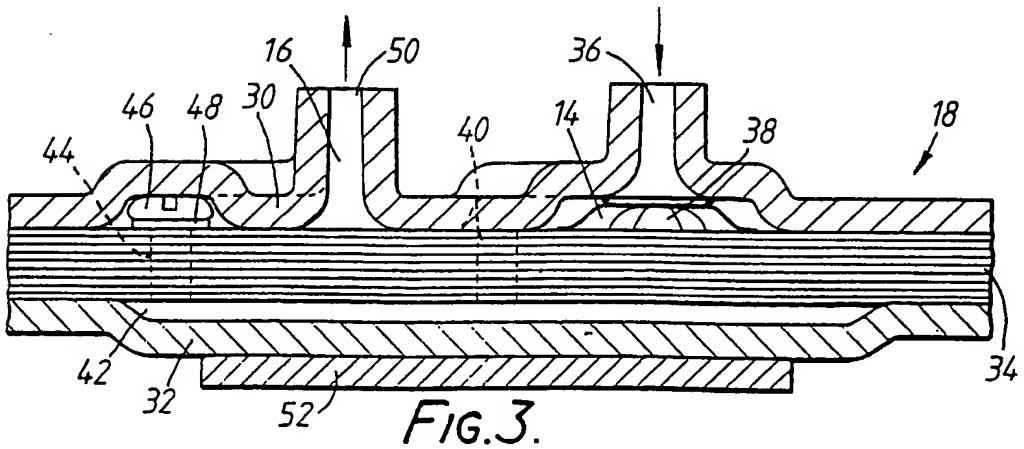


FIG. 3.

2/2

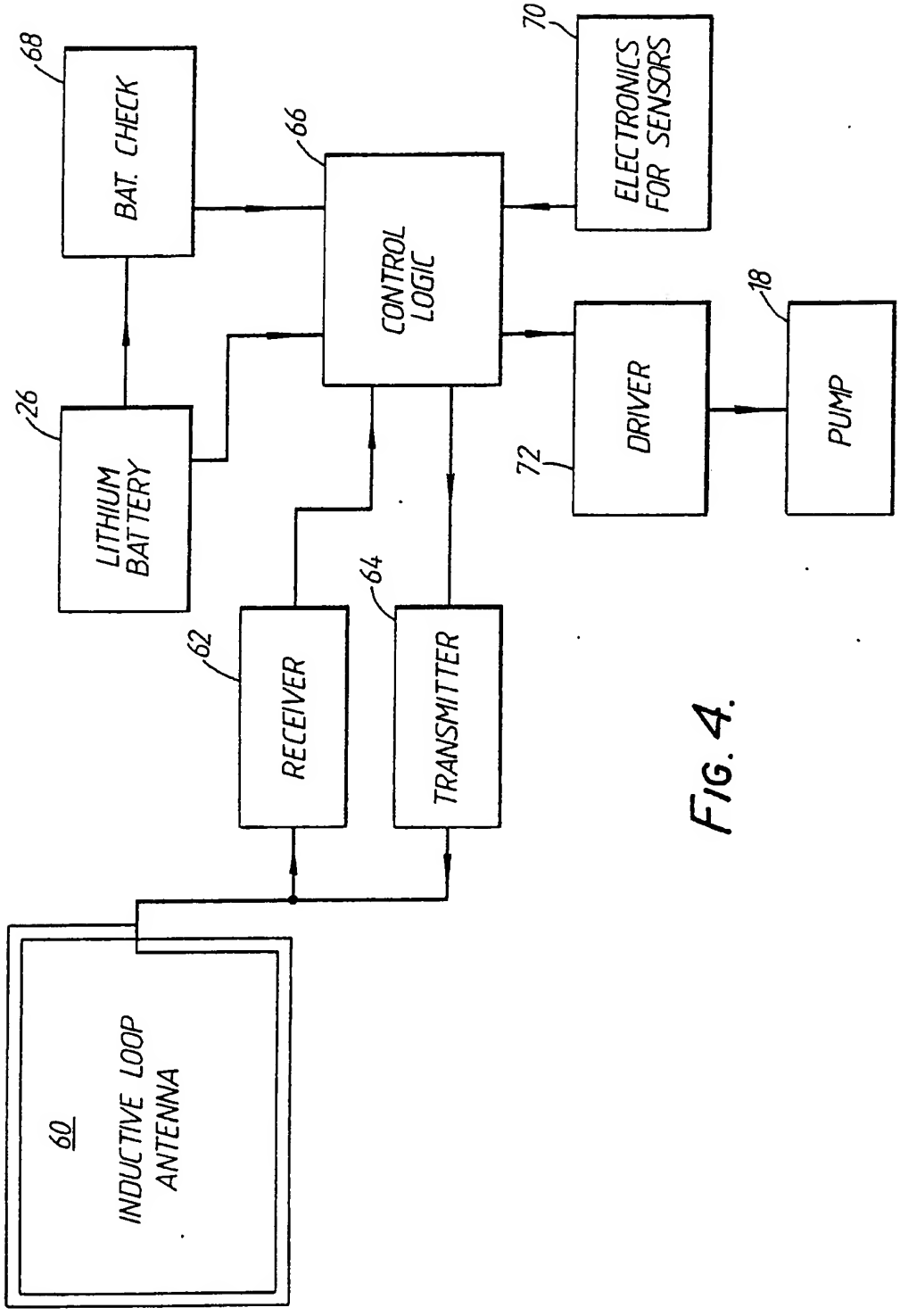

68
BAT. CHECK
66
CONTROL LOGIC
70
ELECTRONICS FOR SENSORS
26
LITHIUM BATTERY
72
DRIVER
18
PUMP
62
RECEIVER
64
TRANSMITTER
60
INDUCTIVE LOOP ANTENNA

FIG. 4.

INTERNATIONAL SEARCH REPORT

International Application No PCT/EP 88/00062

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

IPC[4]: A 61 M 5/14

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
IPC[4]	A 61 M; F 04 B

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
X	EP, A, 0025005 (SCHALDACH) 11 March 1981 see page 13, line 14 - page 14, line 1; figures	1,3,4,5
A		8,9,10
	--	
X	US, A, 4596575 (ROSENBERG) 24 June 1986 see column 3, lines 8-30; figures	1-4,6
	--	
A	EP, A, 0112585 (CONSOLIDATED CONTROLS CORPORATION) 4 July 1984 see page 5, lines 26-33; figure 1	12
	------	

* Special categories of cited documents: [10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
19th May 1988	16. 06. 88
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	P.C.G. VAN DER PUTTEN

Form PCT/ISA/210 (second sheet) (January 1985)

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. EP 8800062

SA 20328

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 09/06/88
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A- 0025005	11-03-81	DE-A,B,C 2933799	26-02-81
US-A- 4596575	24-06-86	None	
EP-A- 0112585	04-07-84	US-A- 4486190	04-12-84
		US-A- 4557726	10-12-85
		CA-A- 1224101	14-07-87